

CLAIMS

We claim:

- 5 1. A method of inhibiting recurrence of a tumor in a subject, comprising: administering a therapeutically effective amount of an agent to the subject in order to block an immunosuppressive effect of transforming growth factor (TGF)- β in the subject, wherein the subject is at risk for recurrence of the tumor, and wherein the agent neutralizes an activity of TGF- β , thereby inhibiting recurrence of the tumor in the subject.
- 10 2. The method of claim 1, wherein the agent is a monoclonal antibody specific for TGF- β and wherein the monoclonal antibody is obtained from hybridoma 1D11.16 (ATCC Accession No. HB 9849).
- 15 3. The method of claim 1, wherein the agent comprises an antagonist, an antibody, a chemical compound, a small molecule, a peptide mimetic, a peptide, or a protein.
4. The method of claim 3, wherein the agent comprises an antibody and wherein the antibody is a polyclonal antibody or a monoclonal antibody.
- 20 5. The method of claim 4, wherein the monoclonal antibody is specific for a TGF- β .
6. The method of claim 5, wherein the anti-TGF- β antibody inhibits TGF- β from binding a TGF- β receptor.
- 25 7. The method of claim 1, wherein the subject is a human.
8. The method of claim 1, wherein the tumor is benign or malignant.
- 30 9. The method of claim 1, wherein the tumor comprises a carcinoma, a sarcoma, a leukemia, a lymphoma, or a tumor of the nervous system.
10. The method of claim 1, wherein the tumor comprises a breast tumor, a liver tumor, a pancreatic tumor, a gastrointestinal tumor, a colon tumor, a uterine tumor, a ovarian tumor, a cervical tumor, a testicular tumor, a brain tumor, a skin tumor, a melanoma, a retinal tumor, a lung tumor, a kidney tumor, a bone tumor, a prostate tumor, a nasopharyngeal tumor, a thyroid tumor, a leukemia, or a lymphoma.

11. The method of claim 1, wherein the agent is administered intravenously, subcutaneously, intradermally, or intramuscularly.
12. The method of claim 1, wherein administering the therapeutically effective amount of the agent results in a lack of tumor growth *in vivo* or *in vitro*.
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13. The method of claim 1, wherein blocking the immunosuppressive effect of the TGF- \square results in increased immunosurveillance by lymphocytes of the subject.
- 10 14. The method of claim 13, wherein the lymphocytes comprise T cells or B cells.
- 15 15. The method of claim 13, wherein the lymphocytes include T cells, and the T cells comprise a cytotoxic T lymphocyte (CTL), a CD8 $^{+}$ CTL, a CD4 $^{+}$ cell, a CD4 $^{+}$ CD1d-restricted T cell, an NKT cell, or a combination thereof.
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16. The method of claim 13, wherein increased immunosurveillance is measured by an increased biological activity of the lymphocyte.
- 20 17. The method of claim 16, wherein the increased activity of the lymphocyte is measured by a CTL assay.
18. The method of claim 17, wherein the CTL assay comprises a chromium release assay.
- 25 19. The method of claim 1, wherein administering comprises contacting a TGF- β receptor with the agent, thereby neutralizing the activity of the TGF- β .
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20. The method of claim 19, wherein the agent comprises an antagonist, an antibody, a small molecule, a chemical compound, a peptide mimetic, a peptide or a protein.
21. The method of claim 19, wherein the agent inhibits TGF- β receptor signaling.
- 35 22. The method of claim 1, wherein administering comprises contacting a downstream signaling molecule of the TGF- β receptor with the agent.
23. The method of claim 22, wherein the agent comprises an antagonist, an antibody, a small molecule, a chemical compound, a peptide mimetic, a peptide or a protein.

24. The method of claim 22, wherein the downstream signaling molecule comprises a Smad protein or a Smad complex DNA-binding co-factor.

25. A method of inhibiting recurrence of a tumor in a subject, comprising:
5 administering a therapeutically effective amount of a monoclonal antibody specific for TGF- β to the subject in order to block an immunosuppressive effect of TGF- β in the subject, wherein the subject is at risk for recurrence of the tumor, and wherein the monoclonal antibody is obtained from hybridoma 1D11.16 (ATCC Accession No. HB 9849) and neutralizes an activity of TGF- β , thereby inhibiting recurrence of the tumor in the subject.

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26. A method of enhancing an activity of an immune cell to inhibit recurrence of a tumor, comprising:

15 contacting a TGF- β receptor-expressing immune cell with an agent that blocks a TGF- β signaling pathway, wherein blocking the TGF- β signaling pathway results in increased tumor immunosurveillance by the TGF- β receptor-expressing immune cell, thereby enhancing the activity of the immune cell to inhibit recurrence of the tumor.

27. The method of claim 26, wherein the TGF- β receptor-expressing immune cell is a T cell or a B cell.

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28. The method of claim 26, wherein the TGF- β receptor-expressing immune cell includes T cells and the T cells comprise a CTL, a CD8 $^{+}$ CTL, a CD4 $^{+}$ cell, a CD4 $^{+}$ CD1d-restricted T cell, or an NKT cell.

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29. The method of claim 26, wherein the agent comprises an antagonist, an antibody, a small molecule, a chemical compound, a peptide mimetic, a peptide or a protein.

30. The method of claim 29, wherein contacting a TGF- β receptor-expressing immune cell with an agent comprises contacting a TGF- β or a TGF- β receptor.

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31. The method of claim 30, wherein the agent contacting the TGF- β comprises an anti-TGF- β monoclonal antibody that is obtained from hybridoma 1D11.16 having ATCC Accession No. HB 9849.

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32. A method of enhancing an immune response in a subject to inhibit recurrence of a tumor, comprising:

administering to the subject a therapeutically effective amount of an agent that blocks a TGF- β signaling pathway, wherein blocking the TGF- β signaling pathway results in increased tumor immunosurveillance in the subject, thereby enhancing the immune response in the subject to inhibit recurrence of a tumor.

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33. The method of claim 32, wherein the immune response is a T cell response.

34. The method of claim 33, wherein the T cell response comprises a CTL response, a CD8 $^{+}$ CTL response, a CD4 $^{+}$ T cell response, a CD4 $^{+}$ CD1d-restricted T cell response or an NKT cell response.

35. The method of claim 32, wherein the agent comprises an antagonist, an antibody, a small molecule, a chemical compound, a peptide mimetic, a peptide or a protein.

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36. The method of claim 35, wherein the agent contacts a TGF- β or a TGF- β receptor.

37. The method of claim 36, wherein the agent comprises an anti-TGF- β monoclonal antibody that is obtained from hybridoma 1D11.16 (ATCC Accession No. HB 9849).

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38. The method of claim 32, wherein the subject is a human.

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39. A method for screening for an agent that inhibits tumor recurrence, comprising: contacting a TGF- β receptor-expressing immune cell with TGF- β ; contacting the TGF- β receptor-expressing immune cell with an agent; and assaying for a decrease in activity of TGF- β signaling in the TGF- β receptor-expressing immune cell, as compared to a TGF- β receptor-expressing control immune cell, wherein the control immune cell is not contacted with the agent, thereby screening for an agent that inhibits tumor recurrence.

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40. The method of claim 39, further comprising assaying for an increase in activity of the TGF- β receptor-expressing immune cell.

41. The method of claim 39, wherein the TGF- β receptor-expressing immune cell is a CTL.

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42. The method of claim 41, wherein the increase in activity of the CTL is measured by a CTL assay.

43. The method of claim 39, wherein the decrease in activity of TGF- β signaling comprises decreased phosphorylation of a Smad protein, decreased nuclear translocation of a Smad protein, or decreased DNA binding of a Smad complex.

5 44. The method of claim 40, wherein the increase in activity of the TGF- β receptor-expressing immune cell comprises increased immunosurveillance.

45. The method of claim 44, wherein increased immunosurveillance comprises increased CTL activity.